UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/662,052	09/15/2000	Vandana Yajnik	5986/1G098-US1	4993

7590 03/22/2002

Darby & Darby PC
805 Third Avenue
New York, NY 10022

EXAMINER	
SOUAYA, JEHANNE E	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 03/22/2002

7

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/662,052	Yajnik et al
Examiner	**Art Unit**
Jehanne Souaya	1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jan 10, 2002* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above, claim(s) *9 and 11-20* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-8 and 10* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 4
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

1. It should be noted that the art unit designation for the examiner has changed from 1655 to 1634.

2. Applicant's request for a corrected filing receipt has been received and entered. The appropriate changes were made.

Election/Restriction

3. Applicant's election with traverse of Group I, claims 1-8 and 10 in Paper No. 6 is acknowledged. The traversal is on the ground(s) that Claim 9 is dependent on claim 6 in Group I, and if claim 6 is found allowable, then claim 9 should be found allowable. With regard to claim 9, the groups are patentably distinct as set forth in the previous restriction requirement. However, should claim 6 be found allowable, the examiner will rejoin claim 9 with group I. The response also traverses that claims 15-18 are dependent upon claim 7 of Group I, and if claim 7 is found allowable, than claims 15-18 should be allowable as well. This argument has been thoroughly reviewed but was not found persuasive because, as set forth in the previous restriction requirement, the claims are patentably distinct because the nucleic acid of group I can be used to design probes and primers for the detection of NRIF3 which is materially different and requires different reagents, reaction conditions, and reaction parameters from the test system and method of identifying a compound that modulates thyroid hormone receptor or retinoid X receptor of group V. Further, the claims in group V encompass transgenic animals which can be used in animal research models, and methods of using transgenic animals, and are patentably distinct

from the polynucleotides, vectors and cells of group I as they are structurally and functionally different.

The requirement is still deemed proper and is therefore made FINAL.

An action on the merits of claims 1-8 and 10 follows.

Priority

4. Applicant's claim for priority under 35 USC 119(e) to provisional application 60/154,347 has been noted. The instant claims have been awarded the benefit of the earlier filing date (September 17, 1999) of the 60/154,347 application as the subject matter in the claims was disclosed in the earlier filed provisional application.

Drawings

5. This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

Claim Rejections - 35 USC § 101

6. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claim 10 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claim 10 recites "a nucleic acid" instead of "an isolated nucleic molecule". As the claim does not recite an upper length limitation for the claimed nucleic acid,

such a recitation would encompass a human chromosome in a human cell that has not been manipulated by the hand of man, thus a product of nature.

Claim Rejections - 35 USC § 112

Indefinite

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 2-3 and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 2, 3, and 10 are indefinite as it is unclear if the recitation of "as depicted in" is meant to encompasses nucleic acid sequences comprising a sequence "within" SEQ ID NO 3, or which encodes a sequence "within" SEQ ID NO 4, or only if the full length sequences are intended (as in "nucleic acid comprising a sequence that encodes...an amino acid sequence consisting of SEQ ID NO 4" or a "nucleic acid sequence comprising a nucleotide sequence consisting of SEQ ID NO 3"). If the latter is the case, the claims should be amended to "consisting of" instead of "as depicted in". If the former is the case, it should be noted that claims 2 and 3 do not necessarily further limit claim 1 as claims 2 and 3 need only contain enough of the C-terminal end of SEQ ID NO 4 such that the LXXIL motif is present.

B) Claim 10 is indefinite in the recitation of "stringent conditions" as this language encompasses different reaction conditions such that the degree of complementarity needed to achieve hybridization between the nucleic acid sequence claimed and SEQ ID NO 3 is unclear. Stringent conditions can encompass conditions of "low stringency", "moderate stringency", and "high stringency". The claim does not make clear what conditions are encompassed by the language and therefore the metes and bounds of the claim are unclear,

C) Claim 10 is indefinite as the claim recites "a nucleic acid" instead of "an isolated nucleic molecule". As the claim does not recite an upper length limitation for the claimed nucleic acid, such a recitation would encompass a human chromosome in a human cell that has not been manipulated by the hand of man, thus a product of nature. It is unclear if that is applicant's intent. If it is, such a recitation is directed to non-patentable subject matter.

Written Description

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 1-8 and 10 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection is set forth on the interpretation of claim 1 that the LXXIL motif (SEQ ID NO 2) is not the only structural feature of the claimed nucleic acid molecule responsible for the function set forth in the claim (binds in a ligand dependent manner to thyroid hormone receptor [TR] and retinoid X receptor [RXR] but does not interact with retinoic acid receptor [RAR], vitamin D receptor [VDR], progesterone receptor [PR], glucocorticoid receptor [GR], and estrogen receptor [ER] in a yeast two hybrid assay system or in vitro or both). The claims are not supported by an adequate written description since neither the claims nor the specification set forth what other structural features of an NRIF3 molecule are needed to exhibit the claimed function. As presently written, the claim is drawn to a molecule whose only structural limitation is the presence of an LXXIL motif in the C terminal domain of the molecule. This recitation encompasses a large number of sequences, including genomic sequences, coding sequences, and allelic variants from any source, that have not been described in the specification as the specification does not define NRIF3 to be only SEQ ID NO 4. The specification teaches that the C terminal LXXIL motif is not the only structural feature responsible for the claimed function (see p. 52, lines 16-25), therefore the recitation of this single structural feature is not representative of the broad genus of nucleic acids encompassed by the claims. The specification teaches a single NRIF3 sequence, consisting of the nucleic acid sequence of SEQ ID NO 3 (which encodes the polypeptide of SEQ ID NO 4), however, from the description in the

specification as to the function of NRIF3, the specification does not make clear what other structural features of NRIF3 are necessary to perform the claimed function.

The specification teaches that SEQ ID NO 4 contains a novel LXXIL motif at the C-terminal end. The specification teaches that an LXXLL signature motif, which has been found to be present in the receptor interacting domain of many identified coactivators, was found in SEQ ID NO 4, at the N-terminal end of the polypeptide. The specification teaches that prior art structural and functional studies has revealed that the LXXLL motif and its nearby flanking amino acids are involved in direct contact with a hydrophobic cleft of the target surface presented by ligand bound, ligand binding domains of nucleic receptors, and that therefore, it was thought that perhaps 1) the LXXLL motif and surrounding amino acids are involved in mediating receptor specific interaction of NRIF3, or 2) another region of NRIF3 (alone or in concert with the LXXLL motif) were important for mediating the distinct receptor specificity exhibited by the NRIF3 of SEQ ID NO 4 (bridging paragraph of pp 49 and 50). With regard to these possibilities, the specification shows: 1) studies with alternative splice variants of NRIF3 (SEQ ID NO 4), which do not contain the C-terminal LXXIL motif, showed that the interaction with liganded TR or RXR was completely abolished and thus that the unique C-terminal domain in SEQ ID NO 4 was essential for its specific interaction with TR and RXR, and that the N-terminal LXXLL motif and it's flanking sequences are not sufficient to allow for detectable receptor interactions (p. 50, lines 9-23); 2) mutating the first leucine in the LXXLL motif to an alanine only reduces the interaction with TR by about 4 fold and with RXR by about 14 fold (bridging para of page 50

and 51); 3) fusing the C-terminal domain of NRIF3 (NCD) with a LexA DNA binding domain showed (referred to as LexA-NCD) (LexA alone does not interact with receptor ligand binding domains) a strong ligand dependent interaction when the ligand binding domain of TR and RXR were present in a yeast two hybrid system, suggesting that the NRIF3 C-terminal domain can directly interact with the LBDs of TR and RXR in a ligand dependent manner (p. 52, lines 2-15); 4)However, LexA-NCD also showed efficient interaction with the ligand binding domain of RAR in ligand dependent manner (contrary to what is found for SEQ ID NO 4), showing that it is possible that another region of NRIF3 with the sequence of SEQ ID NO 4 may contribute to the observed receptor specificity of NRIF3 and/or that the specificity is determined by the overall three dimensional structure of NRIF3 (p. 52, lines 16-25).

Thus, the specification teaches that while the LXXIL motif is essential for the receptor specificity exhibited by SEQ ID NO 4, other regions of SEQ ID NO 4 are also needed for this specificity, and it is not known what these regions are. Therefore, as exhibited by the results from the specification, the single structural limitation of the claimed invention, LXXIL sequence in the C-terminal end of the molecule, is not representative of the broad genus of nucleic acid molecules encompassed by the claims. Further, the skilled artisan would not know what other sequences were encompassed by the recitation in the claims, other than by SEQ ID NO. It is noted that this rejection also applies to claims 2 and 3 as 1) the recitation of "depicted in SEQ ID NOS 3 and 4" does not necessarily further limit claim 1, and 2) it is unclear from the written description in the specification as to how much of the sequence "depicted in" SEQ ID NOS 3 (or

the polypeptide of SEQ ID NO 4) is representative of the broadly claimed genus of polynucleotides. It is noted that since SEQ ID NOS 1-3 are not supported by adequate written description, vectors and host cells comprising the nucleic acids of claims 1-3 also lack adequate written description. Further, with regard to claim 10, the recitation that the claimed nucleic acid need only hybridize to SEQ ID NO 3 under stringent conditions, encompasses not only a broad genus including genomic sequences, coding sequences, and allelic variants from any source, but also mutants of SEQ ID NO 3 (and therefore SEQ ID NO 4) as well. It is noted that such mutants encompass an altered amino acid at every position of SEQ ID NO 4, and at the very least, altered motifs of SEQ ID NO 4 as well as altered flanking regions of motifs. As the specification expressly teaches that it is possible that another region of NRIF3 with the sequence of SEQ ID NO 4 [other than the LXXIL motif] may contribute to the observed receptor specificity of NRIF3 and/or that the specificity is determined by the overall three dimensional structure of NRIF3 (p. 52, lines 16-25), the single mutant with altered functional activity (leucine to alanine mutation of the first leucine in the LXXLL N terminal motif) is not representative of the large genus of polypeptides with altered functional activity encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of

ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NOS: 3 and 4, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993), and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.

Accordingly, the specification does not provide a written description of the invention of claims 1-8 and 10.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claim 10 is rejected under 35 U.S.C. 102(b) as being anticipated by Leberer et al (WO 98/18927; May 7, 1998).

Claim 10 recites a nucleic acid that need only have a minimum of 20 bases (no upper length limitation is recited in the claims) and need only hybridize to a nucleic acid having a sequence as "depicted in" SEQ ID NO 3, under non specified stringent conditions. The phrase "depicted in" is being interpreted to encompass sequences "within" SEQ ID NOS 3. Leberer teaches (fig. 7) a nucleic acid sequence, wherein the complement of the nucleic acid sequence has 45.9% similarity to nucleotides 112-575 of SEQ ID NO 3. Since the claim does not recite any specific hybridization or wash conditions, and the claim does not recite any functional limitation of the claimed nucleic acid that would distinguish it from the sequence taught by Leberer, the sequence taught by Leberer anticipates the claimed invention.

Conclusion

14. No claims are allowable, although allowable subject matter does exist. SEQ ID NOS 3 and 4 are free of the prior art.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Souaya whose telephone number is (703)308-6565. The examiner can normally be reached Monday-Friday from 9:00 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jehanne Souaya

Jehanne Souaya
Patent examiner
Art Unit 1634
March 18, 2002